

Changes during the 2-year extension period (Months 36 to 60):

During Years 4 and 5, the 5- and 10-mg groups experienced significant increases of 0.97 ($p \leq 0.010$), and 0.94 ($p \leq 0.010$) percent in lumbar spine BMD, respectively. The placebo/10-mg group had an increase of 6.36% ($p \leq 0.001$). The 0.26% increase in the 20-/5-mg group was not significant. The increase in lumbar spine BMD observed in the 10-mg group was not significantly different from the increases in the 5- and 20-/5-mg groups.

The data are summarized in the table below:

Alendronate Treatment	n	Mean (Observed)		Percent Change From Month 36				Pairwise Comparison	
		Month 36	Month 60	Mean	SD	Adjusted Mean	95% Interval	5 mg	10 mg
Placebo/10 mg	269	0.75	0.80	6.36***	5.34	6.41	(5.84, 6.97)		
5 mg	130	0.79	0.79	0.97**	4.11	0.98	(0.19, 1.76)		
10 mg	147	0.81	0.82	0.94**	3.73	1.04	(0.31, 1.78)	0.902	
20/5 mg	131	0.81	0.81	0.26	3.67	0.34	(-0.45, 1.12)	0.246	0.187

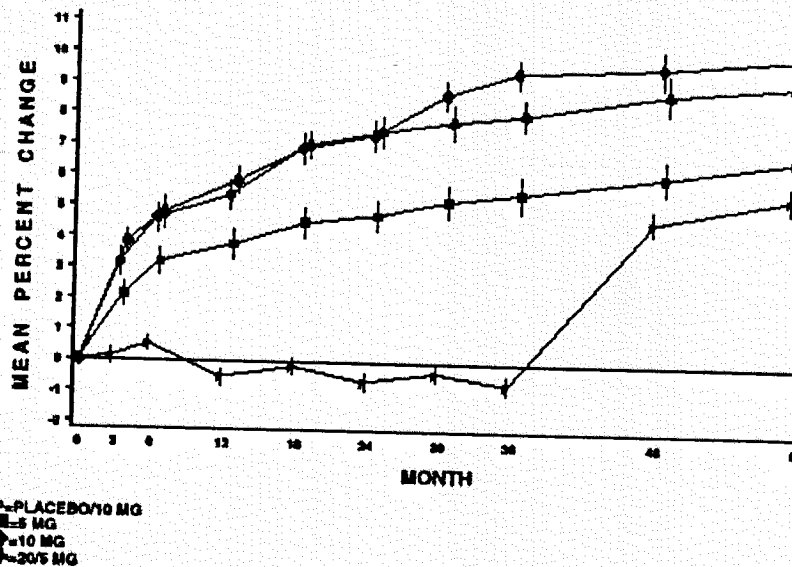
,* Within-treatment p-value: ≤ 0.010 and ≤ 0.001 , respectively.
 Treatment-by-protocol interaction p-value: 0.281.
 Pooled SD: 4.42.
 Overall p-value: < 0.001 .
 Mean difference 10 mg relative to 5 mg: 0.03, 95% CI: -1.07 to 1.02.

Per-protocol results were similar to the intention-to-treat analyses and are presented by the sponsor in Appendices [4.30.1; 4.30.2]. Summaries of percent change from Month 24 at Month 60 in BMD and BMC are in Appendices [4.10.1; 4.10.6], respectively.

The results of BMD analyses performed on individual studies (035-10 and 037-10) were essentially the same for the changes over 5 years. For Protocol 035-10:

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Mean Percent Change (\pm SE) in Lumbar Spine BMD
(Intention-to-Treat Approach)
(Protocol 035-10)



The data are summarized in the table below. For the % change from baseline to Month 60:

Analysis of Percent Change in Lumbar Spine BMD From Baseline at Month 60
(Intention-to-Treat Approach)
(Protocol 035-10)

Alendronate Treatment	n	Mean (Observed)		Percent Change From Baseline				Pairwise Comparison	
		Baseline	Month 60	Mean	SD	Adjusted Mean	LSD Interval	5 mg	10 mg
Placebo/10 mg	127	0.75	0.79	5.45***	4.71	5.16	(4.50, 5.82)		
5 mg	63	0.73	0.78	6.67***	4.74	6.45	(5.55, 7.36)		
10 mg	68	0.75	0.82	10.01***	5.88	9.88	(9.01, 10.75)	<0.001	
20/5 mg	57	0.74	0.81	9.11***	5.93	8.85	(7.90, 9.80)	0.011	0.264

*** Within-treatment p-value: ≤ 0.001 .
Treatment-by-center interaction p-value: 0.458.
Pooled SD: 5.08.
Overall p-value: <0.001.
Mean difference 10 mg relative to 5 mg: 3.34, 95% CI: 1.59 to 5.09.
Data Source: [4.37.5; 4.37.6]

For the % change in BMD from Month 36 to Month 60 in this study, the 10-mg group missed statistical significance:

Analysis of Percent Change in Lumbar Spine BMD From Month 36 to Month 60
(Intention-to-Treat Approach)
(Protocol 035-10)

Alendronate Treatment	n	Mean (Observed)		Percent Change From Month 36				Pairwise Comparison	
		Month 36	Month 60	Mean	SD	Adjusted Mean	95% Interval	5 mg	10 mg
Placebo/10 mg	131	0.74	0.79	6.00***	4.84	5.87	(5.14, 6.61)		
5 mg	65	0.77	0.78	1.26**	3.71	1.11	(0.09, 2.12)		
10 mg	70	0.82	0.82	0.62	3.88	0.53	(-0.44, 1.51)	0.418	
20/5 mg	58	0.80	0.81	0.62	3.93	0.61	(-0.47, 1.68)	0.500	0.920

*** Within-treatment p-value: ≤ 0.010 and ≤ 0.001 , respectively.
 Treatment-by-center interaction p-value: 0.747.
 Pooled SD: 4.10.
 Overall p-value: < 0.001 .
 Mean difference 10 mg relative to 5 mg: -0.64, 95% CI: -2.03 to 0.76.

Similar results obtain from individual analysis of Protocol 037-10, as shown in the figure below:

Analysis of Percent Change in Lumbar Spine BMD From Baseline at Month 60
(Intention-to-Treat Approach)
(Protocol 037-10)

Alendronate Treatment	n	Mean (Observed)		Percent Change From Baseline				Pairwise Comparison	
		Baseline	Month 60	Mean	SD	Adjusted Mean	LSI Interval	5 mg	10 mg
Placebo/10 mg	130	0.76	0.81	6.55***	6.49	6.74	(5.92, 7.56)		
5 mg	60	0.76	0.80	6.03***	5.48	6.15	(4.96, 7.34)		
10 mg	74	0.75	0.81	8.82***	5.93	8.91	(7.84, 9.98)	0.016	
20/5 mg	65	0.75	0.81	9.12***	8.66	9.07	(7.93, 10.20)	0.013	0.885

*** Within-treatment p-value: ≤ 0.001 .
 Treatment-by-center interaction p-value: 0.924.
 Pooled SD: 6.49.
 Overall p-value: 0.011.
 Mean difference 10 mg relative to 5 mg: 2.79, 95% CI: 0.57 to 5.00.

For the changes from Months 36 to 60:

Analysis of Percent Change in Lumbar Spine BMD From Month 36 to Month 60
(Intention-to-Treat Approach)
(Protocol 037-10)

Alendronate Treatment	n	Mean (Observed)		Percent Change From Month 36				Pairwise Comparison	
		Month 36	Month 60	Mean	SD	Adjusted Mean	95% Interval	5 mg	10 mg
Placebo/10 mg	138	0.76	0.80	6.70***	5.78	6.87	(6.05, 7.70)		
5 mg	65	0.80	0.80	0.68	4.49	0.81	(-0.36, 1.98)		
10 mg	77	0.80	0.81	1.23**	3.58	1.49	(0.42, 2.57)	0.390	
20/5 mg	73	0.81	0.81	-0.02	3.45	0.12	(-0.98, 1.22)	0.390	0.075

*** Within-treatment p-value: ≤ 0.010 and ≤ 0.001 , respectively.
 Treatment-by-center interaction p-value: 0.793.
 Pooled SD: 4.69.
 Overall p-value: < 0.001 .
 Mean difference 10 mg relative to 5 mg: 0.56, 95% CI: -1.00 to 2.11.

Comments: Here, the 10-mg group, but not the 5-mg group, achieved statistical significance in BMD increases during the extension period. Again, pairwise comparisons showed no statistical differences between the responses of the 10- and 5-mg groups during this 2-year period. Thus the pooled data demonstrated that each of the two groups increased BMD during the 2-year extension, but that the differences between the two groups in this respect were not statistically significant. When the data were analyzed for each protocol separately, in one the 5-mg group achieved a statistically significant increase over the 2-year period, and in the other the 10-mg group achieved this increase. In no analysis was there any difference between the two groups in responses in (%) BMD over this period.

In any case, all three analyses (pooled, and each protocol separately) clearly show that spinal BMD increased significantly over the 5 years of the study and that the differences between the 5-mg and 10-mg groups were significant throughout this time period.

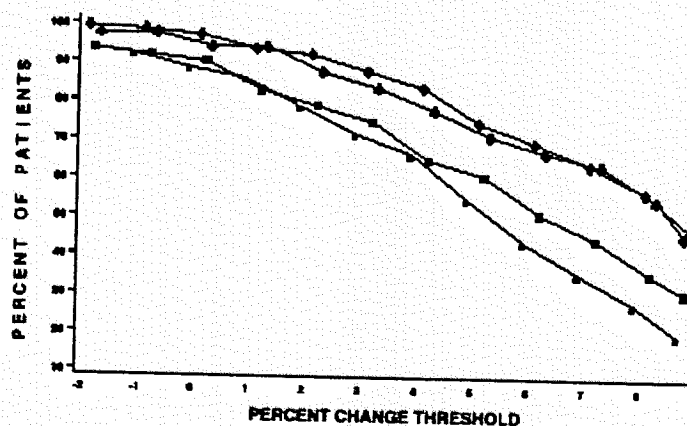
Further comments: In studies of this type it is important to define the percent of patients who responded to treatment. One cannot define this number precisely, but it is usually possible to determine the number (or %) of patients who achieved a given response or greater. The sponsor performed this analysis, and the data, displayed below, demonstrate that only 16% of patients treated with 10 mg alendronate failed to achieve an increase of 4% in BMD, or greater. Compared with the other three treatment groups (placebo/10-, 5-, and 20-/5-mg), the alendronate 10-mg group consistently had a higher percent of patient exceeding each threshold response level.

Percent Change in Lumbar Spine BMD From Baseline to Month 60
(Intention-to-Treat Approach)
(Pooled 035/037)

Alendronate Treatment	n	Percent of Patients Having BMD Change Exceeding											
		-2%	-1%	0%	1%	2%	3%	4%	5%	6%	7%	8%	9%
Placebo/10 mg	257	94.9	92.2	88.7	86.0	78.6	71.6	66.5	54.9	44.0	35.8	28.0	19.8
5 mg	123	93.5	91.9	90.2	82.9	78.9	74.8	65.0	61.0	51.2	44.7	35.8	30.9
10 mg	142	99.3	98.6	97.2	93.7	92.3	88.0	83.8	74.6	69.7	64.1	57.0	47.2
20/5 mg	122	97.5	97.5	94.3	94.3	87.7	83.6	77.9	71.3	67.2	63.9	54.9	45.9

A graphic illustration of these data is given below:

Percent of Patients With 60-Month Change in Lumbar Spine BMD
Exceeding Thresholds Ranging -2 to 9%
(Intention-to-Treat Approach)
(Pooled 035/037)



□ PLACEBO/10 MG
● 5 MG
▲ 10 MG
◆ 20/5 MG

Data Source: [4.37.5; 4.37.6]

Femoral Neck BMD:

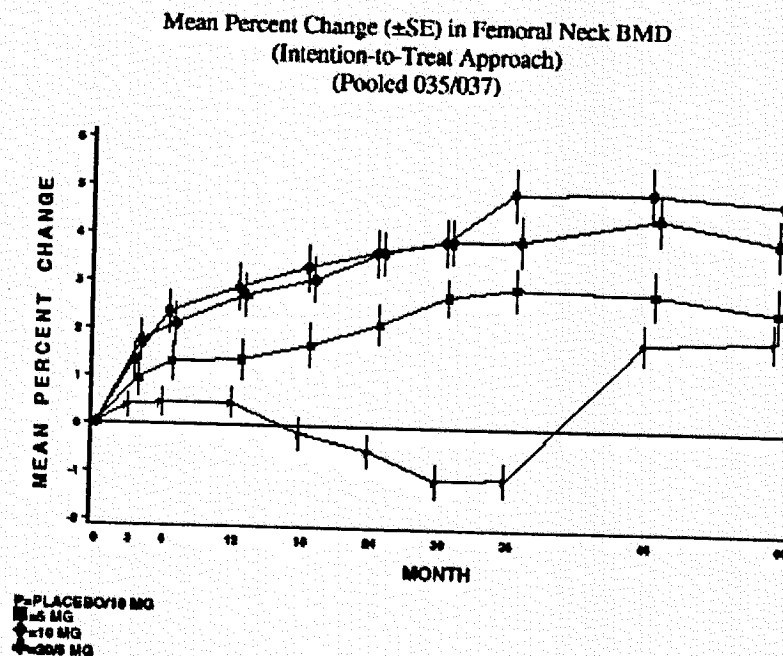
Qualitatively similar results were obtained for analysis of BMD changes at the femoral neck. Within each of the 4 treatment groups, patients showed a significant ($p \leq 0.001$) increase in femoral neck BMD from baseline to Month 60. The mean increases were 1.9, 2.5, 4.8, and 4.0% in the placebo/10-, 5-, 10-, and 20-/5-mg groups, respectively. The increase in the 10-mg group was significantly greater ($p = 0.004$) than that observed in the 5-mg group.

Femoral neck BMD in the placebo/10-mg group decreased during the first 3 years of treatment with placebo, then sharply increased during Year 4, and continued to increase during Year 5 with alendronate treatment. There was an increase of 0.5 and 0.3% from Month 36 to Month 60 in the 10- and 20-/5-mg groups; however, these increases were not significant. The 5-mg alendronate

group experienced a decrease of -0.5% from Months 36 to 60, which was not significant. The percent changes from Months 36 to 60 in the alendronate 10- and 5-mg groups were not significantly different.

The per-protocol results differ from the intention-to-treat results for the Months 36-60 analysis: there was a significant ($p \leq 0.050$) decrease in mean percent change in femoral neck BMD (-0.82%) in the 5-mg group during Years 4 and 5. Per-protocol results for analysis of change over 5 years coincide with intention-to-treat results.

For pooled data, the mean % changes in femoral neck BMD in the 4 treatment groups is shown in the figure below:



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A summary of the statistical analysis of data for the 5-year period is given in the table below:

Analysis of Percent Change in Femoral Neck BMD From Baseline at Month 60
(Intention-to-Treat Approach)
(Pooled 035/037)

Alendronate Treatment	n	Mean (Observed)		Percent Change From Baseline				Pairwise Comparison	
		Baseline	Month 60	Mean	SD	Adjusted Mean	LSD Interval	5 mg	10 mg
Placebo/10 mg	227	0.66	0.67	1.92***	6.12	2.16	(1.60, 2.73)	.	.
5 mg	113	0.65	0.67	2.51***	5.92	2.74	(1.96, 3.52)	.	.
10 mg	122	0.63	0.66	4.77***	6.27	4.95	(4.20, 5.70)	0.004	.
20/5 mg	119	0.65	0.68	3.97***	5.66	3.96	(3.20, 4.72)	0.119	0.193

*** Within-treatment p-value: ≤ 0.001 .

Treatment-by-protocol interaction p-value: 0.323.

Pooled SD: 5.87.

Overall p-value: < 0.001 .

Mean difference 10 mg relative to 5 mg: 2.27, 95% CI: 0.76 to 3.77.

Pooled data for the interval, 36-60 months are shown below:

Analysis of Percent Change in Femoral Neck BMD From Month 36 to Month 60
(Intention-to-Treat Approach)
(Pooled 035/037)

Alendronate Treatment	n	Mean (Observed)		Percent Change From Month 36				Pairwise Comparison	
		Month 36	Month 60	Mean	SD	Adjusted Mean	95% CI	5 mg	10 mg
Placebo/10 mg	253	0.65	0.67	3.03***	5.30	3.12	(2.49, 3.76)	.	.
5 mg	128	0.67	0.67	-0.45	4.02	-0.25	(-1.12, 0.61)	.	.
10 mg	142	0.67	0.67	0.45	4.73	0.54	(-0.27, 1.36)	0.179	.
20/5 mg	128	0.68	0.68	0.32	5.25	0.50	(-0.37, 1.37)	0.215	0.943

*** Within-treatment p-value: ≤ 0.001 .

Treatment-by-protocol interaction p-value: 0.801.

Pooled SD: 4.83.

Overall p-value: < 0.001 .

Mean difference 10 mg relative to 5 mg: 0.91, 95% CI: -0.25 to 2.06.

Individual analyses of each protocol showed no significant differences from results obtained from analysis of pooled data.

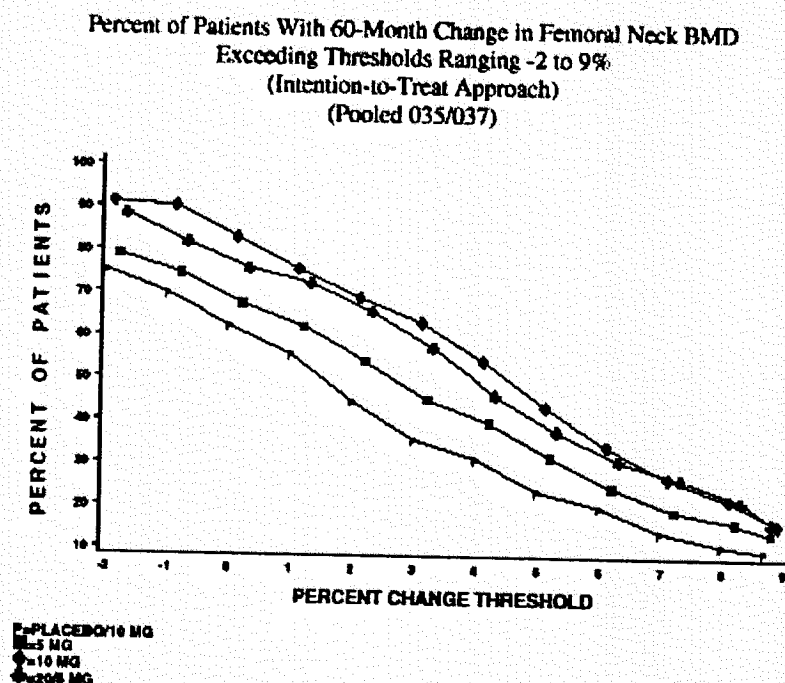
Per protocol results of analysis of the 5-year data were essentially the same as those from the ITT analysis. However, per protocol results for Months 36-60 differed from the ITT results: there was a significant ($p < 0.05$) decrease in mean % change in femoral neck BMD, in the 5-mg group, of -0.82%.

A response analysis showed that the percent of patients who experienced a positive (i.e., $> 0\%$) percent change in femoral neck BMD from baseline at Month 60 was 62.1, 67.3, 82.8, and 75.6% in the placebo/10-, 5-, 10-, and 20-/5-mg groups, respectively. These data are summarized below:

Percent Change in Femoral Neck BMD From Baseline to Month 60
(Intention-to-Treat Approach)
(Pooled 035/037)

Alendronate Treatment	n	Percent of Patients Having BMD Change Exceeding											
		-2%	-1%	0%	1%	2%	3%	4%	5%	6%	7%	8%	9%
Placebo/10 mg	227	74.9	69.6	62.1	55.5	44.5	35.7	31.3	23.8	20.3	14.5	11.5	10.1
5 mg	113	78.8	74.3	67.3	61.9	54.0	45.1	39.8	31.9	24.8	19.5	16.8	14.2
10 mg	122	91.0	90.2	82.8	75.4	68.9	63.1	54.1	43.4	34.4	27.0	22.1	16.4
20/5 mg	119	88.2	81.5	75.6	72.3	65.5	57.1	46.2	37.8	31.1	26.9	21.8	16.8

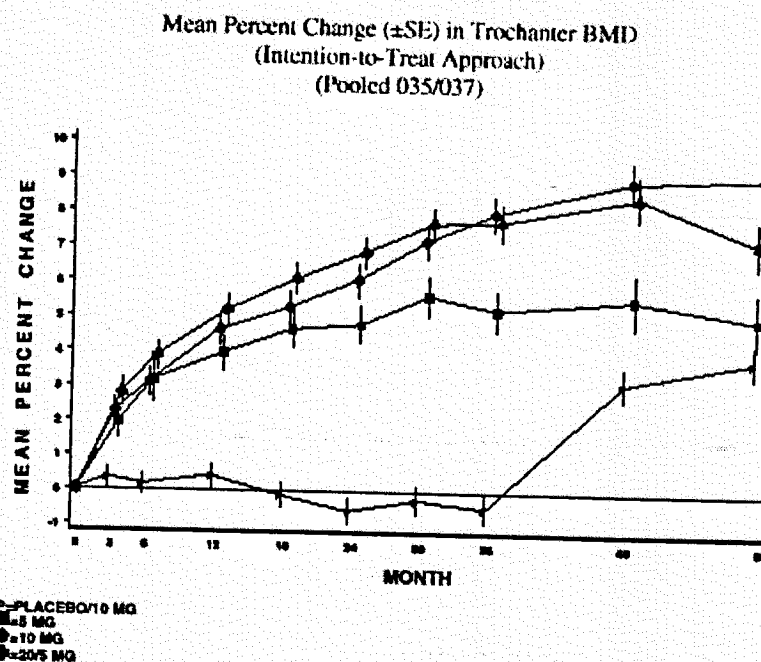
These responder data are represented graphically in the sponsor's figure below:



Trochanter BMD:

At the trochanter, between baseline and Month 60, all doses of alendronate were associated with significant increases ($p \leq 0.001$) in trochanter BMD. Mean increases of 3.8, 5.0, 9.1, and 7.2% were seen in the placebo/10-, 5-, 10-, and 20-/5-mg groups, respectively. At the end of Year 5, the increase in the 10-mg group was significantly greater than that of the 5-mg group ($p < 0.001$).

Data (pooled) for the 5-year period are shown in the graph below:



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As seen in this figure, trochanter BMD in the placebo/10-mg group slowly decreased during the first 3 years, then sharply increased during the fourth year, and changed moderately during the fifth year. There was a significant increase of 4.3 and 0.9% in the placebo/10-mg ($p \leq 0.001$) and 10-mg ($p \leq 0.050$) treatment groups, respectively, from Months 36 to 60. In the alendronate 5- and 20-/5-mg groups, there were decreases from Month 36 at Month 60 that were not statistically significant.

At all time points, per-protocol results were similar to the intention-to-treat results.

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A summary of the statistical analysis of these data is presented in the table below:

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Analysis of Percent Change in Trochanter BMD From Baseline at Month 60
(Intention-to-Treat Approach)
(Pooled 035/037)

Alendronate Treatment	n	Mean (Observed)		Percent Change From Baseline				Pairwise Comparison	
		Baseline	Month 60	Mean	SD	Adjusted Mean	LSI Interval	5 mg	10 mg
Placebo/10 mg	224	0.57	0.59	3.84***	6.98	4.09	(3.41, 4.77)	.	.
5 mg	112	0.56	0.58	5.01***	8.38	5.14	(4.20, 6.08)	.	.
10 mg	121	0.55	0.60	9.09***	6.38	9.13	(8.23, 10.03)	<0.001	.
20/5 mg	117	0.55	0.59	7.19***	7.09	6.93	(6.01, 7.84)	0.057	0.017

*** Within-treatment p-value: ≤ 0.001 .

Treatment-by-protocol interaction p-value: 0.779.

Pooled SD: 7.01.

Overall p-value: < 0.001 .

Mean difference 10 mg relative to 5 mg: 4.08, 95% CI: 2.27 to 5.89.

Data Source: [4.37.5; 4.37.6]

As shown in the table below, there was a small, statistically non-significant decrease in BMD in the 5-mg treatment group from Months 36-60, but a significant increase in the 10-mg group during this interval. The difference in response between the 5- and 10-mg groups was statistically significant.

Analysis of Percent Change in Trochanter BMD From Month 36 to Month 60
(Intention-to-Treat Approach)
(Pooled 035/037)

Alendronate Treatment	n	Mean (Observed)		Percent Change From Month 36				Pairwise Comparison	
		Month 36	Month 60	Mean	SD	Adjusted Mean	95% CI	5 mg	10 mg
Placebo/10 mg	249	0.57	0.59	4.28***	5.10	4.67	(3.99, 5.34)	.	.
5 mg	126	0.59	0.58	-0.46	6.30	-0.17	(-1.08, 0.74)	.	.
10 mg	142	0.60	0.60	0.88*	4.39	1.12	(0.26, 1.98)	0.040	.
20/5 mg	127	0.59	0.59	-0.56	4.75	-0.33	(-1.24, 0.58)	0.799	0.02

*** Within-treatment p-value: 0.050 and 0.001, respectively.

Treatment-by-protocol interaction p-value: 0.987.

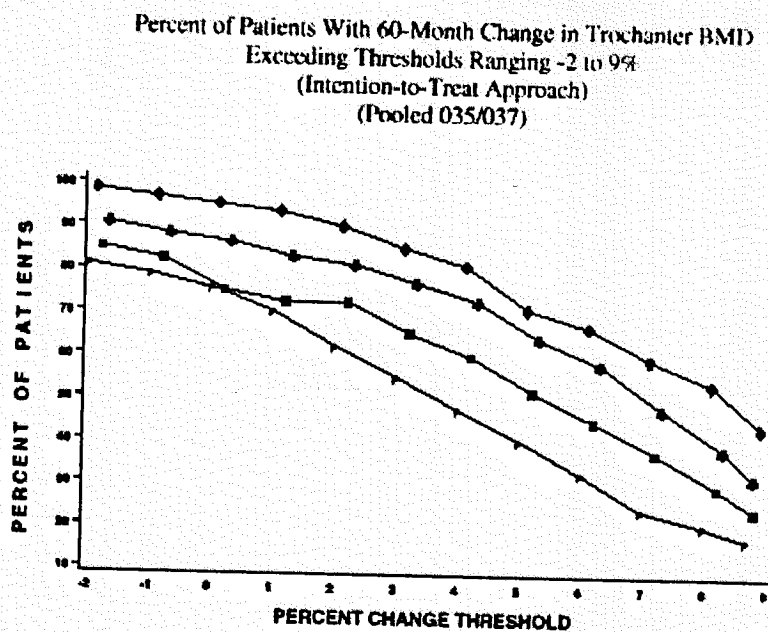
Pooled SD: 5.06.

Overall p-value: < 0.001 .

Mean difference 10 mg relative to 5 mg: 1.33, 95% CI: 0.12 to 2.55.

Data Source: [4.37.5; 4.37.6]

The percent of patients with a positive ($> 0\%$) change in trochanter BMD from baseline to Month 60 was 75.4, 75.0, 95.0, and 86.3% in the placebo/10-, 5-, 10-, and 20-/5-mg groups, respectively. The data for response rate as a percent of change are presented below:



Data Source: [4.37.5; 4.37.6]

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Total body BMD:

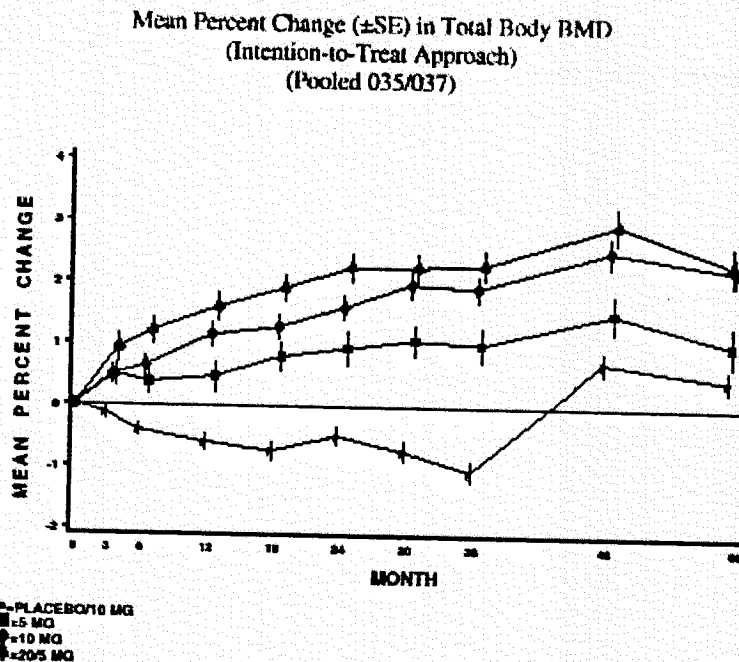
During the five-year period, all four treatment groups had significant increases in total body BMD over baseline. The increases were: 0.5 ($p < 0.050$), 1.0 ($p < 0.010$), 2.2 ($p < 0.001$), and 2.3% ($p < 0.001$) for the placebo/10-, 5-, 10-, and 20-/5-mg groups, respectively.

The increase in BMD in the 10-mg group was significantly ($p < 0.001$) higher than in the 5-mg group.

During the two-year extension period, the 5-, 10, and 20-/5-mg treatment groups experienced statistically nonsignificant changes in BMD (-0.02, 0.19, and -0.19%, respectively). During the fifth year, all 4 treatment groups showed a numerical decrease in total body BMD that was not statistically significant.

Per-protocol results of the between group analyses were similar to the ITT results. There was no significant treatment-by-protocol interaction.

The mean percent change in total body BMD in the 4 treatment groups over the 60-month period is represented in the following figure:



Data Source: [4.37.5; 4.37.6]

Analysis of percent change in total body BMD from baseline to month 60 is displayed in the table below:

Analysis of Percent Change in Total Body BMD From Baseline at Month 60
(Intention-to-Treat Approach)
(Pooled 035/037)

Alendronate Treatment	n	Mean (Observed)		Percent Change From Baseline				Pairwise Comparison	
		Baseline	Month 60	Mean	SD	Adjusted Mean	LSD Interval	5 mg	10 mg
Placebo/10 mg	158	0.95	0.95	0.45*	2.29	0.68	(0.41, 0.95)	.	.
5 mg	82	0.93	0.94	1.02**	2.82	1.17	(0.81, 1.54)	.	.
10 mg	94	0.94	0.96	2.24***	2.18	2.37	(2.04, 2.71)	<0.001	.
20/5 mg	86	0.93	0.95	2.32***	2.90	2.26	(1.91, 2.61)	0.003	0.735

*, **, *** Within-treatment p-value: ≤ 0.050 , ≤ 0.010 , ≤ 0.001 , respectively.
 Treatment-by-protocol interaction p-value: 0.796.
 Pooled SD: 2.28.
 Overall p-value: <0.001.
 Mean difference 10 mg relative to 5 mg: 1.22, 95% CI: 0.54 to 1.90.
 Data Source: [4.37.5; 4.37.6]

Analysis of data for the Month 36-60 interval is shown in the table below:

Analysis of Percent Change in Total Body BMD From Month 36 to Month 60
(Intention-to-Treat Approach)
(Pooled 035/037)

Alendronate Treatment	n	Mean (Observed)		Percent Change From Month 36				Pairwise Comparison	
		Month 36	Month 60	Mean	SD	Adjusted Mean	95% CI	5 mg	10 mg
Placebo/10 mg	177	0.94	0.95	1.50***	2.16	1.40	(1.11, 1.68)		
5 mg	86	0.94	0.94	-0.02	1.75	-0.02	(-0.42, 0.38)		
10 mg	103	0.96	0.96	0.19	1.92	0.16	(-0.20, 0.53)	0.479	
20/5 mg	94	0.95	0.95	-0.19	1.88	-0.26	(-0.64, 0.12)	0.354	0.089

*** Within-treatment p-value: ≤ 0.001 .
 Treatment-by-protocol interaction p-value: 0.594.
 Pooled SD: 1.74.
 Overall p-value: ≤ 0.001 .
 Mean difference 10 mg relative to 5 mg: 0.21, 95% CI: -0.28 to 0.71.
 Data Source: [4.37.5; 4.37.6]

Comments: The small declines in total body BMD seen in the 5-mg and 20/5-mg groups during the two-year extension were not statistically significant.

One-Third Forearm (Radius + Ulna) BMD:

Comment: As mentioned above, this proximal forearm site is made up of >95% cortical bone and is the only such bone site that is measured in this study. This measurement gives some insight into the effects of alendronate on non-weight-bearing cortical bone.

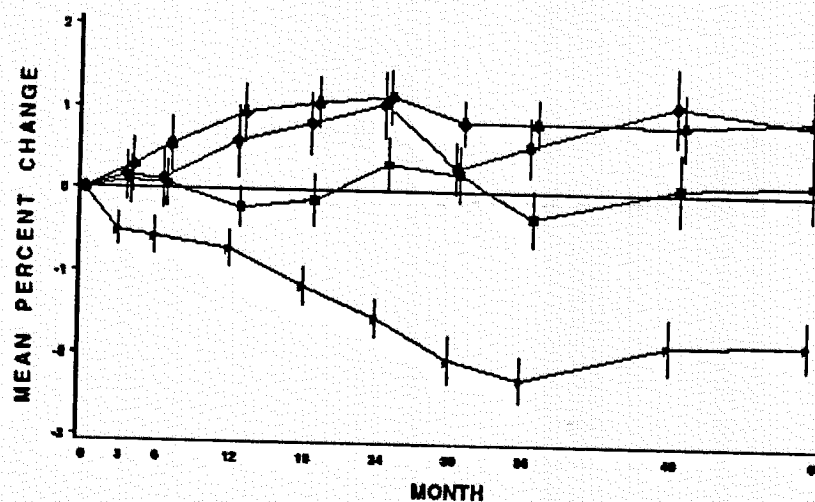
At this site, the increases in bone were not as great in magnitude over the 60-month period, and one group (placebo/10mg) lost bone over this time period.

As shown in the figure and two tables below, there was a significant decrease of -1.8% in one-third forearm BMD at Month 60, compared to baseline, in the placebo/10-mg group ($p < 0.001$). As expected, the mean BMD in this group fell steadily during the first 36 months. This trend was reversed following the introduction of alendronate at this time, and the BMD in this group rose by 0.56% ($p < 0.050$) during the two-year extension. However, the BMD in this group remained well below baseline, and the final mean was -1.8%.

In both the 10- and 20/5-mg groups there was a significant increase ($p < 0.050$) of 0.9% at Month 60, compared to baseline. The 0.1% increase observed in the 5-mg treatment group was not statistically significant. The BMD rose from Months 36 to 60 in the 5-, 10-, and 20-/5-mg groups (by 0.3, 0.6, and 0.03%, respectively); however, these increases were not significant.

There was no treatment-by-protocol interaction, and the results of the per-protocol analysis were similar to those for the ITT approach.

Mean Percent Change (\pm SE) One-Third Distal Forearm (Radius + Ulna) BMD
(Intention-to-Treat Approach)
(Pooled 035/037)



P=PLACEBO/10 MG
■=5 MG
◆=10 MG
●=20/5 MG

Data Source: [4.37.5; 4.37.6]

Analysis of the 60-month data:

Analysis of Percent Change From Baseline at Month 60 in One-Third Forearm (Radius+Ulna) BMD
(Intention-to-Treat Approach)
(Pooled 035/037)

Alendronate Treatment	n	Mean (Observed)		Percent Change From Baseline				Pairwise Comparison	
		Baseline	Month 60	Mean	SD	Adjusted Mean	LSD Interval	5 mg	10 mg
Placebo/10 mg	133	0.55	0.54	-1.82***	3.45	-2.13	(-2.55, -1.70)	.	.
5 mg	71	0.54	0.54	0.14	3.47	-0.24	(-0.81, 0.32)	.	.
10 mg	73	0.54	0.54	0.85*	3.38	0.65	(0.10, 1.21)	0.106	.
20/5 mg	70	0.53	0.54	0.92*	3.26	0.74	(0.18, 1.30)	0.080	0.879

*.,*** Within-treatment p-value: 50.0%, 50.001, respectively.
 Treatment-by-protocol interaction p-value: 0.680.
 Pooled SD: 3.29.
 Overall p-value: <0.001.
 Mean difference: 10 mg relative to 5 mg: 0.71, 95% CI: -0.37 to 1.79.
 Data Source: [4.37.5; 4.37.6]

Analysis of the one-third forearm BMD data from 36-60 months:

Analysis of Percent Change From Month 36 to Month 60 in One-Third Forearm (Radius+Ulna) BMD
(Intention-to-Treat Approach)
(Pooled 035/037)

Alendronate Treatment	n	Mean (Observed)		Percent Change From Month 36				Pairwise Comparison	
		Month 36	Month 60	Mean	SD	Adjusted Mean	95% CI	5 mg	10 mg
Placebo/10 mg	151	0.54	0.54	0.56*	3.15	0.32	(-0.11, 0.76)	.	.
5 mg	81	0.54	0.54	0.28	2.48	0.09	(-0.49, 0.67)	.	.
10 mg	78	0.55	0.55	0.55	2.96	0.42	(-0.17, 1.00)	.	.
20/5 mg	75	0.54	0.54	0.03	2.83	0.11	(-0.49, 0.70)	.	.

* Within-treatment p-value: ≤ 0.050 .
Treatment-by-protocol interaction p-value: 0.945.
Pooled SD: 2.57.
Overall p-value: 0.806.
Mean difference 10 mg relative to 5 mg: 0.26, 95% CI: -0.54 to 1.07.

BMD data from other secondary sites:

Data from assessments at other secondary anatomic sites (Ward's triangle, ultra-distal forearm, and total hip) are presented in the Appendices. Graphical representations of these data are presented below:

APPENDIX 4.14

4.14.1: Alendronate Phase III Osteopenia Bone Density Study (Pooled 035/037)
Ward's BMD

Mean Percent Change \pm SE of the Mean
"Intention-to-Treat" Approach

